510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:
k121790

B. Purpose for Submission:
New Device

C. Measurand:
Cardiac troponin I (cTnI)

D. Type of Test:
Quantitative paramagnetic-particle chemiluminescent immunoassay

E. Applicant:
Beckman Coulter, Inc.

F. Proprietary and Established Names:
Access AccuTnI+3 Reagent, Access AccuTnI+3 Calibrator, UniCel DxI 800 Access Immunoassay System

G. Regulatory Information:

1. Regulation section:
   21 CFR 862.1215 Creatine phosphokinase/creatine kinase or isoenzymes test system
   21 CFR 862.1150 Calibrator
   21 CFR 862.2160 Discrete photometric chemistry analyzer for clinical use

2. Classification:
   Class II (21 CFR 862.1215 and 21 CFR 862.1150),
   Class I (21 CFR 862.2160)

3. Product code:
   MMI, Immunoassay method, troponin subunit
   JIT, Calibrator, secondary
   JJE, Analyzer, chemistry (photometric, discrete), for clinical use

4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See indication(s) for use below

2. Indication(s) for use:
   The Access AccuTnI+3 Reagent is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the UniCel DxI Immunoassay Systems to aid in the diagnosis of myocardial infarction.

   The Access AccuTnI+3 Calibrators are intended to calibrate the Access AccuTnI+3 Reagent for the quantitative determination of cardiac troponin I (cTnI) levels in human serum and plasma using the UniCel DxI Immunoassay Systems to aid in the diagnosis of myocardial infarction.

   The UniCel DxI 800 Access Immunoassay System is an *in vitro* diagnostic device used for the quantitative, semi-quantitative, or qualitative determination of various analyte concentrations found in human body fluids.

3. Special conditions for use statement(s):
   For prescription use only, for *in vitro* diagnostic use

4. Special instrument requirements:
   Performance data was generated using the UniCel DxI 800 Access Immunoassay System

I. Device Description:

Component	Description
The Access AccuTnI+3 Reagent	Consists of two reagent packs, each contains the following: • Paramagnetic particles coated with mouse monoclonal anti-human cardiac troponin I (cTnI) suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA) matrix, < 0.1% sodium azide and 0.1% ProClin 300. • 0.1N NaOH • TRIS buffered saline, surfactant, < 0.1% sodium azide and 0.1% ProClin 300. • Mouse monoclonal anti-human cTnI alkaline phosphatase conjugate diluted in ACES buffered saline with surfactant, BSA matrix, protein (bovine, goat, and mouse), < 0.1% sodium azide and 0.25% ProClin 300.
The Access AccuTnI+3 Calibrators	Consists of ready-to-use, liquid, multi-point calibrators for use with the Access AccuTnI+3 Reagent. • Six vials containing zero, approximately 0.2, 0.9, 3.7, 20 and 80 ng/mL of recombinant cardiac troponin I complex in a buffered BSA matrix, with surfactant,

	< 0.1% sodium azide and 0.1% ProClin 300. The calibrators are sold separately.
Instrument	The UniCel DxI 800 Access Immunoassay System is a microcomputer controlled, random-access and continuous-access instrument. The instrument performs enzyme immunoassays utilizing paramagnetic particle solid phase and chemiluminescent detection. A luminometer measures the amount of light generated by the reaction. The UniCel DxI 800 Access Immunoassay System is designed to be used with numerous different immunoassays. The system software was designed such that immunoassays can be added to the system without changing the system software. A separate assay-specific protocol file, the APF, is loaded into the system. The APF contains all assay specific parameters used to process a particular assay. To correct thermal sensitivity from ambient temperature fluctuations that could affect the accuracy of troponin test results, the sponsor developed a software algorithm that normalizes troponin results. This solution was implemented through a combination of system and operating software changes.

J. Substantial Equivalence Information:

Predicate device name	510(k) number
ADVIA Centaur TnI-Ultra Assay	k053020
ADVIA Centaur TnI-Ultra Calibrator	k053020
Beckman Coulter UniCel DxI 800 Access Immunoassay System	k023764

Comparison with predicate:

Similarities		
Item	Access AccuTnI+3 Reagent	Predicate Device (k053020)
Intended Use	*in vitro* diagnostic method for the quantitative measurement of cardiac TnI in serum and plasma	Same
Assay Principle	Chemiluminescent sandwich immunoassay	Same
Test System	Automated immunoassay instrument	Same
Primary Reagent Materials	Solid phase magnetic particles, anti cTnI antibodies	Same

Differences		
Item	Access AccuTnI+3 Reagent	Predicate Device (k053020)
Indications For Use	Not for risk stratification use	For risk stratification use
Sample Types	Serum and heparinized plasma	Serum, heparinized plasma and EDTA plasma
Instrument	UniCel DxI Access Immunoassay Systems with thermal algorithm capability	ADVIA Centaur System
Specific Reagent Materials	Mouse monoclonal anti-human cTnI alkaline phosphatase conjugate, magnetic particles coated with mouse monoclonal anti-human cTnI	Polyclonal goat anti-cTnI antibody labeled with acridinium ester, 2 biotinylated mouse monoclonal anti-cTnI antibodies, magnetic particles conjugated with streptavidin
Acute Myocardial Infarction (AMI) Cut-Off	0.03 ng/mL validated based on clinical trial outcome	0.9 ng/mL per WHO-defined cut-off
Upper Reference Limit	99th percentile below the LoQ	99th percentile of 0.04 ng/mL

Similarities		
Item	Access AccuTnI+3 Calibrator	Predicate Device (k053020)
Intended Use	Intended to calibrate the Access AccuTnI+3 Reagent	Intended to calibrate the ADVIA Centaur TnI-Ultra assay

Differences		
Item	Access AccuTnI+3 Calibrator	Predicate Device (k053020)
Calibrator Materials	Recombinant troponin complex in buffered BSA	Bovine cTnI in goat serum
Calibrator Number And Type	Six Liquid: approximately 0, 0.2, 0.09, 3.7, 20 and 80 ng/mL (with no master curve)	Two lyophilized: high and low (use with Master Curve)

K. Standard/Guidance Document Referenced (if applicable):

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline (EP5-A2)
- Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical

Approach; Approved Guideline (EP6-A)
- Interference Testing in Clinical Chemistry; Approved Guideline (EP7-A2),
- Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline (EP17-A2)
- Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline (EP25-A)
- Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline (C28-A3c)

L. Test Principle:

The Access AccuTnI+3 Reagent is a two-site immunoenzymatic ("sandwich") assay. Monoclonal anti-cTnI antibody conjugated to alkaline phosphatase is added to a reaction vessel along with a surfactant-containing buffer and sample. After a short incubation, paramagnetic particles coated with monoclonal anti-cTnI antibody are added. The human cTnI binds to the anti-cTnI antibody on the solid phase, while the anti-cTnI antibody - alkaline phosphatase conjugate reacts with different antigenic sites on the cTnI molecules. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate Lumi-Phos* 530 is added to the vessel and light generated by the reaction is measured. The light production is directly proportional to the concentration of cTnI in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The sponsor evaluated precision in several studies based on CLSI EP5-A2.

The first 3 studies were conducted at one of 3 ambient temperature conditions. The first 2 studies performed at 18 and 28°C were performed internally each on 1 instrument and 1 reagent pack lot; however, instruments and reagent lots were different for the 2 studies. A low spiked patient pool (lp), 3 commercial controls (c), and one high patient pool (hp), were assayed in replicates of 2, 2 shifts per day, 2 runs per shift, for a total of 21 shifts (42 runs) over 13 days for a total of 84 test results (n) per sample.

The third study was performed externally under existing laboratory conditions (measured temperatures ranged from 21.3ºC to 23.6ºC). Five commercial controls (ranging from 0.04 to 13.6 ng/mL) were run in duplicate, 2 runs per day for 20 days for a total of 40 runs for a total of 80 test results (n) per sample. This study was performed using 1 reagent lot and 1 instrument.

The fourth study was a confirmation study that was run across 8 multiple ambient temperatures ranging from 18 to 28ºC. The sponsor used a low spiked patient pool (lp), 3 commercial controls (c), and one high patient pool (hp). These samples were

tested in duplicate per run in a total of 48 runs over 14 days for a total of 96 test results (n) per sample. The coefficients of variability (CV) were calculated. One reagent lot and 1 instrument were used in this study. The data from this study is presented below:

Mean (ng/mL)	n	Imprecision (%CV)		
		Between-Temperature	Within-Run + Between-Run (within-temperature)	Total
0.06 (lp)	96	6	7	9
0.87 (c)	96	6	4	7
3.22 (c)	96	1	3	3
13.13 (c)	94	4	5	6
50.24 (hp)	96	3	3	4

The following data are presented in the labeling: In all tables, Within-Lab imprecision includes within-run and between-run variability.

Mean (ng/mL)	n	Imprecision (%CV)		
		Within-Run	Between-Run	Within-Lab
0.05 (lp)	84	5	7	8
0.51 (c)	84	2	4	4
3.19 (c)	84	2	6	6
13.83 (c)	84	4	3	5
58.04 (hp)	84	4	4	5

The sponsor also determined the precision of the device using 3 low-level natural patient sample pools, 2 instrument, 2 reagent lots, multiple ambient temperatures ranging from 18 to 28ºC and multiple calibration cycles over 12 days. The samples were assayed in replicates of 2 per run, 2 runs per shift and 2 shifts per day for a total of 576 test results (n) per sample. The results of the study are summarized below (these are also included in the labeling):

Mean (ng/mL)	n	Imprecision (%CV)	
		Within-Lab	Total
0.04	576	6	12
0.42	576	4	7
0.98	576	4	7

Field precision studies: The sponsor performed a precision study in-house to simulate the use of the device by the end user. This study was designed to incorporate different sources of variability that may be found in the field including: the simultaneous running of other assays; variability in test request type (e.g., panel, reflex, stat, and individual testing); variability of ambient temperatures; and variability of instrument age. The sponsor used quality control material for the study,

3 instruments and 1 lot of reagent. The sponsor cycled the temperature of the laboratory from 18 to 28 ºC over the course of 6 hours over 3 days of testing. The samples were assayed in a minimum of 80 replicates on each instrument across the 3 days of testing. The results of this study are summarized below:

Instrument	Sample	Mean (ng/mL)	Total Imprecision (%CV)
1	1	0.06	6
	2	0.58	5
	3	1.85	3
	4	0.36	4
	5	8.04	5
2	1	0.06	4
	2	0.58	5
	3	1.84	4
	4	0.35	3
	5	7.83	4
3	1	0.05	5
	2	0.55	5
	3	1.74	4
	4	0.34	5
	5	7.62	4

External Field precision study: The sponsor performed this study to evaluate the precision of the device at external sites. Commercially available quality control materials were run in duplicate per run with 3 lots of reagents on 4 instruments at 4 external sites over 7 days (sample 1 fell below the LoQ of the assay and is not listed). Each site ran a minimum of 18 runs for a total of at least 40 replicates per sample, per reagent lot. One instrument was used at each site. The results of the study are summarized below:

Reagent lot 1

Sample	Means (ng/mL) observed at the 4 sites	Within-Lab %CVs observed at the 4 sites
2	0.04	6 to 7
3	0.55 to 0.62	4 to 6
4	0.90 to 0.96	3 to 6
5	2.31 to 2.49	4 to 6
6	13.23 to 13.75	3 to 6

Reagent lot 2

Sample	Means (ng/mL) observed at the 4 sites	Within-Lab %CVs observed at the 4 sites
2	0.04	5 to 10
3	0.54 to 0.60	5 to 7
4	0.89 to 0.98	4 to 7
5	2.30 to 2.51	4 to 7
6	12.89 to 14.79	3 to 6

Reagent lot 3

Sample	Means (ng/mL) observed at the 4 sites	Within-Lab %CVs observed at the 4 sites
2	0.04	6 to 9
3	0.055 to 0.60	4 to 6
4	0.91 to 1.00	5 to 6
5	2.27 to 2.54	5 to 7
6	13.22 to 15.20	3 to 8

b. *Linearity/assay reportable range:*
Linearity was evaluated in accordance with the CLSI EP6-A guideline utilizing 2 reagent lots and 2 instruments at 3 different temperature conditions (from 18 to 28 ºC) using lithium heparin plasma samples spiked with native cardiac troponin I analyte. The high and low samples were tested neat in replicates of 8 while each of the 7 intermediate mixtures was tested in replicates of 4. A total of 12 analyses were performed. The polynomial fit was significant for 10 of the 12 analyses but the maximum deviation from nonlinearity was 12%. The sponsor claims acceptable linearity across the reportable range (0.03 to 80 ng/mL).

High Dose Hook Effect: The sponsor demonstrated that there was no high dose hook effect from the concentration of the S5 calibrator (≈80 ng/mL) to 2,094 ng/mL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The Access AccuTnI+3 Calibrators are standardized to an internal standard.

Calibrators are value assigned using primary reference curves and verified using quality control material and patient samples that must meet pre-determined specifications.

Calibrator stability: The sponsor claims that the calibrators are stable for 12 months when stored unopened at -20°C. Once opened, the sponsor claims that the calibrators are stable for 60 days when stored at 2 to 8°C.

d. *Detection limit:*
The limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) studies were performed following the recommendations in EP17-A2. Testing was

performed over 3 days using 3 reagent lots, 3 instruments and 3 different calibration and run temperature conditions (from 18 to 28 ºC).

To estimate the LoB, 4 blank samples were measured in replicates of 10 on each day of testing on each instrument/reagent lot combination at the different temperature conditions. The sponsor claims that the LoB is 0.004 ng/mL.

To estimate the LoD, 6 native lithium heparin plasma samples containing low levels of troponin I analyte were measured in 2 runs of 10 replicates each during each day of testing on each instrument/reagent lot combination at the different temperature conditions. The sponsor claims an LoD of 0.008 ng/mL.

To estimate the LoQ, 11 native lithium heparin plasma samples containing low levels of troponin I analyte were measured in 2 runs of 10 replicates each during each day of testing on each instrument/reagent lot combination at the different temperatures.

The sponsor claims that the LoQ is 0.03 ng/mL with a performance goal of < 20% CV (within-lab). The lowest concentration with a CV (within-lab) < 10% was estimated to be 0.04 ng/mL.

The sponsor provided data demonstrating that the LoQ of the device using serum samples at 3 different temperature conditions (from 18 to 28 ºC) is identical to the LoQ of the device using lithium heparin plasma samples.

The reportable range of the device is 0.03 to 80 ng/mL.

e. Analytical specificity:

Two levels of potential interfering substances were added to lithium heparin plasma pools containing either 0.05 or 0.5 ng/mL troponin. For the controls, the corresponding solvent was added to the lithium heparin plasma pools containing either 0.05 or 0.5 ng/mL troponin. Control troponin samples (control sample) and samples spiked with the potential interferents (test sample) were tested in replicates of 5 (for the 0.5 ng/mL samples) at 3 different temperature conditions (from 18 to 28 ºC) or 10 (for the 0.05 ng/mL samples) and compared. The sponsor used a total of 4 reagent lots and 5 instruments for the studies; however, each individual condition, (paired sample and test, at a given temperature) was tested on one instrument and one reagent lot. The sponsor concluded that the following substances at the listed concentrations did not interfere with the performance of the device.

Substance Added	Highest Concentration Tested	Difference Observed
Acetaminophen	20 mg/dL	≤10%
Acetylsalicylic Acid	65 mg/dL	≤10%
Allopurinol	40 mg/dL	≤10%
Ambroxol	40 mg/dL	≤10%
Ampicillin	5 mg/dL	≤10%

Ascorbic Acid	6 mg/dL	≤10%
Atenolol	1 mg/dL	≤10%
Bilirubin conjugated	40 mg/dL	≤10%
Bilirubin unconjugated	40 mg/dL	≤10%
Biotin	290 ng/mL	≤10%
Caffeine	10 mg/dL	≤10%
Captopril	5 mg/dL	≤10%
Cinnarizine	40 mg/dL	≤10%
Cocaine	2 mg/dL	≤10%
Diclofenac	5 mg/dL	≤10%
Digoxin	200 ng/mL	≤10%
Dopamine	30 mg/dL	≤10%
Erythromycin	20 mg/dL	≤10%
Fibrinogen	1000 mg/dL	≤10%
Furosemide	40 mg/dL	≤10%
Hemoglobin	500 mg/dL	≤10%
Human Serum Albumin	6000 mg/dL	≤10%
Ibuprofen	50 mg/dL	≤10%
Low MW Heparin	28.8 U/mL	≤10%
Methyldopa	2.5 mg/dL	≤10%
Nifedipine	60 µg/dL	≤10%
Nitrofurantoin	6.4 mg/dL	≤10%
Nystatin	2.15 mg/dL	≤10%
Oxytetracycline	24 mg/dL	≤10%
Phenytoin	10 mg/dL	≤10%
Propranolol	500 µg/mL	≤10%
Quinidine	2 mg/dL	≤10%
Simvastatin	20 µg/mL	≤10%
Theophylline	25 mg/dL	≤10%
Triglycerides	3000 mg/dL	≤10%
Trimethoprim	7.5 mg/dL	≤10%
Verapamil	16 mg/dL	≤10%
Warfarin	30 µg/mL	≤10%

Cross-reactivity: To evaluate cross reactivity, the substances shown in the following table were added to lithium heparin plasma pools containing 2 levels of troponin (< 0.03 ng/mL and approximately 0.5 ng/mL). Control and test samples were tested on 5 instruments and 3 reagent lots at 3 temperature conditions (from 18 to 28 ºC) in replicates of 10 for the low troponin samples (<0.03 ng/mL) and replicates of 5 for the high troponin samples (0.05 ng/mL). Each individual condition (paired sample and test, at a given temperature) was tested on one instrument and one reagent lot. For each possible cross-reactant tested, the troponin I concentration (ng/mL) obtained for the spiked sample was compared to the troponin I concentration obtained with the control sample and applied to the following formula: % cross reactivity = [(mean dose of spiked – mean dose of control)/amount of cross reactant spiked] X 100. The

sponsor concluded that the following proteins at the concentration listed did not cross react (defined as < 1% cross reactivity) with the device.

Substance	Concentration Tested (ng/mL)
Actin	1000
Cardiac troponin C	1000
Recombinant human CK-MB	1000
Myoglobin	1000
Myosin	1000
Recombinant human cTnT	250
Skeletal troponin I	1000
Tropomyosin	1000

HAMA/Heterophile antibodies: The sponsor provided results demonstrating that their formulation reduces the effects of HAMA interferents. They include the following in the Limitations of the Procedure section of the Instructions for Use:

"For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies."

f. Assay cut-off:
See section 4 "Clinical cut-off"

2. Comparison studies:

a. Method comparison with predicate device:
Not applicable

b. Matrix comparison:
The sponsor conducted a clinical matrix comparison study to compare 123 matched lithium heparin plasma samples and serum samples randomly selected from among the entire pivotal trial cohort. Results of Passing-Bablok regression analyses of singlicate results are provided below (the sponsor excluded samples with troponin levels below the LoQ from these analyses):

Passing Bablok Regression by Concentration Ranges

Range (ng/mL)	n	Slope (95% CI)	Intercept (95% CI)	Correlation
0.03 to 20	86	1 (1.00 to 1.00)	0.00 (0 to 0)	r = 1.00
0.03 to 5	83	1 (1.00 to 1.00)	0.00 (0 to 0)	r= 0.99
0.03 to 0.4	68	1 (1.00 to 1.00)	0.00 (0 to 0)	r= 0.99

Clinical concordance analysis using 123 matched samples from the pivotal trial cohort was performed between the 2 sample types at the 0.03 ng/mL cut-off and is provided below: The sponsor demonstrated 97% agreement between the lithium heparin plasma samples and serum samples.

Concordance at the 0.03 ng/mL cut-off

	Serum < 0.03	Serum ≥ 0.03	Total
Plasma < 0.03	33	1	34
Plasma ≥ 0.03	3	86	89
Total	36	87	123

An additional matrix comparison study was performed at 3 different temperature conditions (ranging from 18 to 28°C) on 2 instruments using 1 reagent lot. The study included 118 matched serum and lithium heparin plasma samples (not spiked or diluted) which were run at each temperature condition. The following are representative results (of singlicate measurements) of Passing-Bablok regression analysis and are presented in the labeling:

Range (ng/mL)	n	Slope (95% CI)	r value	Intercept (95% CI)
0.03 - 61	118	0.99 (0.98 - 1.00)	1.00	0.00 (-0.01 – 0.00)

3. Clinical studies:

a. Clinical Sensitivity:

A clinical study was performed to evaluate the clinical performance of the device at the different cut-offs. A multicenter prospective study enrolled 1929 patients from Emergency Departments presenting with chest pain or equivalent ischemic symptoms suggestive of Acute Coronary Syndromes. Final diagnoses were adjudicated by an independent panel of expert physicians using criteria consistent with the 2007 Universal Definition of Myocardial Infarction from the ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Serial samples were collected from patients within 9 hours of presentation to the ER. The sample collection times were at baseline, 1 to 3 hours, 3 to 6 hours and 6 to 9 hours after presentation to the ER. Investigators and adjudicators were blinded to the proposed device's results. Adjudicators were also blinded to site diagnoses. All results presented below were based on the adjudicated diagnoses. Testing was performed using lithium heparin plasma samples. The results are summarized below:

Clinical Performance at 0.03 ng/mL (this cut-off was determined in a feasibility study by ROC analysis)

Based on sample collection timepoint:

Interval	Sensitivity		Specificity	
	%	95% CI	%	95% CI
Baseline	84.2 (213/253)	79.1-88.5	90.0 (1508/1675)	88.5-91.4
≥1-3 h	93.5 (116/124)	87.7-97.2	91.0 (923/1014)	89.1-92.7
≥3-6 h	91.1 (143/157)	85.5-95.0	89.2 (839/941)	87.0-91.1
≥6-9 h	93.0 (40/43)	89.9-98.5	90.2(222/246)	85.8-93.7

Interval	Positive Predictive Value		Negative Predictive Value	
	%	95% CI	%	95% CI
Baseline	56.1 (213/380)	50.9-61.1	97.4 (1508/1548)	96.5-98.1
≥1-3 h	56.0 (116/207)	49.0-62.9	99.1 (923/931)	98.3-99.6
≥3-6 h	58.4 (143/245)	51.9-64.6	98.4 (839/853)	97.3-99.1
≥6-9 h	62.5 (40/64)	49.5-74.3	98.7 (222/225)	96.2-99.7

Based on hours since symptom onset:

Interval	Sensitivity		Specificity	
	%	95% CI	%	95% CI
< 8 h	89.7 (148/165)	84.0-93.9	90.8 (902/993)	88.9-92.6
≥ 8 h	91.8 (145/158)	86.3-95.5	89.3 (993/1112)	87.3-91.1

Interval	Positive Predictive Value		Negative Predictive Value	
	%	95% CI	%	95% CI
< 8 h	61.9 (148/239)	55.4-68.1	98.2 (902/919)	97.1-98.9
≥ 8 h	54.9 (145/264)	48.7-61.0	98.7 (993/1006)	97.8-99.3

Clinical Performance at 0.04 ng/mL (lowest measured concentration with a CV (within-lab) <10%)

Based on sample collection timepoint:

Interval	Sensitivity		Specificity	
	%	95% CI	%	95% CI
Baseline	71.9 (182/253)	66.0-77.4	94.1 (1577/1675)	92.9-95.2
≥1-3 h	88.7 (110/124)	81.8-93.7	94.7 (960/1014)	93.1-96.0
≥3-6 h	83.4 (131/157)	76.7-88.9	93.0 (875/941)	91.2-94.5
≥6-9 h	93.0 (40/43)	80.9-98.5	93.9 (231/246)	90.1-96.5

Interval	Positive Predictive Value		Negative Predictive Value	
	%	95% CI	%	95% CI
Baseline	65.0 (182/280)	59.1-70.6	95.7 (1577/1648)	94.6-96.6
≥1-3 h	67.1 (110/164)	59.3-74.2	98.6 (960/974)	97.6-99.2
≥3-6 h	66.5 (131/197)	59.4-73.0	97.1 (875/901)	95.8-98.1
≥6-9 h	72.7 (40/55)	59.0-83.9	98.7 (231/234)	96.3-99.7

Based on hours since symptom onset:

Interval	Sensitivity		Specificity	
	%	95% CI	%	95% CI
< 8 h	83.6 (138/165)	77.1-88.9	94.4 (937/993)	92.7-95.7
≥ 8 h	86.1 (136/158)	79.7-91.1	93.3 (1038/1112)	91.7-94.7

Interval	Positive Predictive Value		Negative Predictive Value	
	%	95% CI	%	95% CI
< 8 h	71.1 (138/194)	64.2-77.4	97.2 (937/964)	96.0-98.1
≥ 8 h	64.8 (136/210)	57.9-71.2	97.9 (1038/1060)	96.9-98.7

Non-MI Patients with troponin I test results above the cut-off
Of the 1676 non-MI patients in the prospective multicenter pivotal trial, 188 (11%) had at least one troponin I test results above the cut-off (0.03 ng/mL) on one or more of the serial draws. Of these 188 patients, 98.4% (185/188) were found to have cardiac conditions such as angina, atrial fibrillation, cardiomyopathy, carditis, heart failure, severe coronary artery disease, tachycardia; or non-cardiac conditions such as renal failure or pulmonary embolism that may result in myocardial damage.

*b. Clinical specificity**:***
See clinical specificity information above in 3a

c. Other clinical supportive data (when a. and b. are not applicable):
Not applicable

4. Clinical cut-off**:**
The cut-off for this assay is 0.03 ng/mL and was determined in a feasibility study by ROC analysis. The sponsor also provided clinical performance information in the package insert at 0.04 ng/mL which is the lowest concentration with a CV (within-lab) <10%.

5. Expected values/Reference range:
   The sponsor conducted a multicenter prospective study to establish the 99th percentile upper reference limit in a population of apparently healthy adults with no known diseases of the cardiovascular system or other serious acute or chronic diseases or infections. Lithium heparin plasma samples were evaluated. Five-hundred twenty seven (527) subjects were enrolled at seven geographically diverse locations. Both male and female subjects were included in the reference range study to determine the 99th percentile upper reference limit.

   The 99th percentile upper reference limit was < 0.03 ng/mL (the LoQ of the assay).

N. Instrument Name:

UniCel DxI 800 Access Immunoassay System

O. System Descriptions:

1. Modes of Operation:
   Micro computer controlled analyzer with random and continuous access.

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?
   Yes __X__ or No ____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?
   Yes _____ or No __X__

2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes__X__or No _____

3. Specimen Identification:
   Bar code or sample information can also be entered manually.

4. Specimen Sampling and Handling:
   Instructions on sample handling are provided in the reagent labeling.

5. Calibration:
   An active calibration curve is required for all tests. For the Access AccuTnI+3 Reagent, calibration is required every 56 days.

6. Quality Control:
   The sponsor recommends that at least two levels of an appropriate quality control material be tested a minimum of once a day. The sponsor also states that quality control testing should be performed in accordance with laboratory accreditation requirements, applicable laws and good laboratory practices.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

The sponsor performed several studies to evaluate the performance of the corrective thermal algorithm designed to correct thermal sensitivity from ambient temperature fluctuations that could affect the accuracy of troponin test results.

Ambient temperature method comparison studies: The sponsor provided data from 2 studies to demonstrate the impact of ambient temperature differences on the test result. These studies focused on troponin concentrations around the cut-offs (0.03 to 0.477 ng/mL for study 1; 0.03 to 0.590 ng/mL for study 2). At least 382 unaltered lithium heparin plasma patient samples were tested at different temperature conditions (ranging from 18 to 28ºC) on multiple instruments using multiple reagent lots. Samples were divided into 3 aliquots, and tested at 3 different temperature conditions (either 18, 22 and 26 ºC or 20, 24 and 28 ºC). Using Passing-Bablok regression analyses comparing the test results obtained at the different temperatures (i.e., 18 vs 26 ºC, 18 vs 22 ºC and 22 vs 26 ºC or 20 vs 28 ºC, 20 vs 24 ºC and 24 vs 28 ºC), the sponsor demonstrated that there was no significant systemic bias observed when comparing test results obtained between 18 and 28°C.

The sponsor performed an additional study using at least 118 lithium heparin plasma patient samples, 2 instruments and 1 lot of reagents. The samples were divided into 3 aliquots and were tested at each of three temperatures (18, 23 and 28 ºC). A calibration curve was established at each of the 3 temperatures. Individual sample results were calculated from the calibration curve established at each temperature (i.e., results generated at 18 ºC were calculated from the calibration curves at 18, 23, and 28 ºC). Using Passing Bablok regression analyses comparing the test results obtained at the different calibration and run temperatures (i.e., 18 vs 23 ºC, 23 vs 28 ºC and 28 vs 18 ºC), the sponsor demonstrated that there was no significant systemic bias observed when comparing test results obtained when samples were run and calibrated at temperatures between 18 and 28°C.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.